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564 Table 1: Major toxicants and carcinogens related to tobacco use

Parent compound	Biomarker/Metabolite	Rationale for inclusion
<b><i>Tobacco-specific N-nitrosamines</i></b>		
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	A potent lung carcinogen (40) and major contributor to cancer risk (34); Group 1 carcinogen (39); WHO Tobreg list: one out of nine toxicant recommended for mandated lowering in tobacco smoke (36)
<b><i>Volatile organic compounds</i></b>		
Acrolein	N-Acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA)	A major contributor to respiratory effects (34, 35); Group 3 carcinogen (41); WHO Tobreg list: one out of nine toxicant recommended for mandated lowering in tobacco smoke (36)
Acrylamide	N-Acetyl-S-(2-carbamoyl-ethyl)-L-cysteine (AAMA)	Group 2A carcinogen (37); a neurotoxin (71)
Acrylonitrile	N-Acetyl-S-(2-cyanoethyl)-L-cysteine (CYMA)	A major contributor to cancer risk (34), highly specific VOC biomarker for tobacco use (33); Group 2B carcinogen (37); WHO Tobreg list: one out of nine toxicant considered high priority for disclosure and monitoring (36)
1,3-Butadiene	N-Acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine (MHBMA3)*	A major contributor to cancer risk (34, 35) ; Group 1 carcinogen (42); WHO Tobreg list: one out of nine toxicant recommended for mandated lowering in tobacco smoke (36)
Ethylene Oxide	N-Acetyl-S-(2-hydroxyethyl)-L-cysteine (HEMA) <sup>†</sup>	Group 1 carcinogen (37)

565 \*More selective metabolite of parent compound than N-Acetyl-S-(3,4-dihydroxybutyl)-L-cysteine (DHBMA) (33);

566 <sup>†</sup>Major urinary metabolite of ethylene oxide exposure, a minor metabolite of acrylonitrile and vinyl chloride exposure  
567 (toxic tobacco smoke constituents); WHO Tobreg - World Health Organisation study group on tobacco product  
568 regulation; VOC – volatile organic compound; International Agency for Research on Cancer (IARC) classification of  
569 carcinogen groups: Group 1 - Carcinogenic to humans; Group 2A - Probably carcinogenic to humans; Group 2B -  
570 Possibly carcinogenic to humans; Group 3 - Not classifiable as to its carcinogenicity to humans; Group 4 - Probably not  
571 carcinogenic to humans

Table 2: Socio-demographic, smoking, physical health and subjective well-being characteristics of study participants

Characteristics	Total (N=181)	Smokers			Ex-smokers		<i>P-value</i>
		Cigarette- only (N=37)	Dual cigarette- NRT users (n=36)	Dual cigarette- EC users (n=36)	NRT- only users (n=36)	EC-only users (n=36)	
Mean age (SD)	37.8 (11.8)	34.4 (14.0)	36.4 (8.5)	39.3 (13.1)	40.3 (11.1)	38.5 (11.1)	0.27
% Female (N)	39.2 (71)	43.2 (16)	61.1 (22)	30.6 (11)	41.7 (15)	19.4 (7)	0.024
% White (N)	72.4 (131)	81.1 (30)	58.3 (21)	75.0 (27)	63.9 (23)	83.3 (30)	0.11
% High school (N)	77.3 (140)	67.6 (25)	83.3 (30)	80.6 (29)	77.8 (28)	77.8 (28)	0.61
% Single (N)	53.6 (97)	70.3 (26)	58.3 (21)	50.0 (18)	36.1 (13)	52.8 (19)	0.10
Mean age started smoking (SD)	17.8 (4.3)	16.6 (3.2)	18.2 (3.4)	17.3 (3.1)	20.3 (6.4)	16.6 (3.2)	0.012
Mean cigarettes per day (SD)*	13.3 (8.7)	13.9 (9.0)	10.8 (4.6)	11.9 (9.6)	14.7 (10.3)	15.9 (8.3)	0.10
Mean proportion of friends/family who smoke (SD)	35.6 (27.5)	50.9 (23.6)	39.8 (24.1)	38.0 (32.4)	33.2 (27.7)	15.6 (15.2)	<0.001
% Recent Illness (N)	23.2 (42)	37.8 (14)	8.3 (3)	19.4 (7)	27.8 (10)	22.2 (8)	0.10
Geometric mean salivary CRP levels, in µg/L (IQR) <sup>†</sup>	1.8 (2.5)	2.0 (3.4)	1.3 (1.1)	1.6 (3.5)	1.9 (2.1) <sup>‡</sup>	2.2 (3.7)	0.86
Mean global life satisfaction (SD) <sup>§</sup>	3.9 (1.0)	4.1 (0.9)	3.8 (1.1)	3.7 (1.1)	3.9 (0.9)	3.9 (1.1)	0.60
Mean happiness levels (SD) <sup>‡</sup>	5.0 (1.5)	4.6 (1.7)	5.6 (1.1)	4.7 (1.7)	5.3 (1.3)	5.0 (1.6)	0.10

<sup>†</sup>Statistical comparison conducted on log-transformed values (not shown); <sup>‡</sup>N=1 missing; <sup>§</sup>Assessed by asking: “All things considered, how satisfied are you with your life as a whole?” with response options (1) “very dissatisfied” to (5) “very satisfied”; <sup>‡</sup>Assessed by asking: “Some people are very generally very happy. They enjoy life regardless of what is going on, getting the most out of everything. To what extent does this characterisation describe you?” with response option from (1) “not at all” to (7) “a great deal”; NRT – nicotine replacement therapy; EC – electronic cigarette; CRP – C-reactive protein; IQR – interquartile range; P-value – omnibus test result, adjusted for the reported comparisons in this table using the false discovery rate (46)

Table 3: Adjusted biomarker levels by group as proportion of cigarette-only smoker levels\*

Parent Compound	Biomarker/Metabolite	Smokers		Ex-smokers	
		Dual cigarette-NRT users (n=36)	Dual cigarette-EC users (n=36)	NRT-only users (n=36)	EC-only users (n=36)
Alkaloids		Percent (95% confidence interval) <sup>†</sup>			
Nicotine	Total nicotine equivalents <sup>‡</sup>	104.2 (64.3-168.9)	156.8 (105.1-233.8)	121.6 (62.5-236.8)	126.9 (82.1-196.2)
	Nicotine <sup>‡</sup>	64.2 (39.2-104.9)	152.2 (90.7-255.1)	135.1 (68.1-268.0)	60.4 (35.8-101.8)
	Cotinine <sup>‡</sup>	46.8 (26.3-83.3)	69.7 (42.1-115.3)	82.1 (42.9-157.3)	75.1 (45.3-124.4)
Tobacco Specific N-Nitrosamines					
4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	57.1 (33.1-98.4)	81.2 (49.7-132.8)	11.6 (6.3-21.3)	2.5 (1.5-4.2)
Volatile Organic Compounds					
Acrolein	N-Acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA)	107.1 (71.8-159.7)	91.2 (60.2-138.2)	35.3 (23.5-53.0)	33.3 (20.9-53.1)
Acrylamide	N-Acetyl-S-(2-carbamoylethyl)-L-cysteine (AAMA)	80.2 (57.9-111.1)	115.9 (80.8-166.1)	45.4 (32.4-63.5)	42.9 (31.1-59.2)
Acrylonitrile	N-Acetyl-S-(2-cyanoethyl)-L-cysteine (CYMA)	85.6 (48.7-150.4)	102.7 (63.7-165.6)	10.5 (5.4-20.6)	2.9 (1.7-4.7)
1,3-Butadiene	N-Acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine (MHBMA3)	101.9 (64.6-160.7)	115.0 (73.2-180.6)	19.9 (12.8-30.7)	11.0 (7.5-16.1)
Ethylene oxide, acrylonitrile, vinyl chloride	N-Acetyl-S-(2-hydroxyethyl)-L-cysteine (HEMA)	86.6 (58.7-127.8)	104.0 (73.9-146.4)	54.2 (38.4-76.5)	43.5 (30.8-61.3)

\*Levels as a proportion of cigarette-only smoker levels are estimated from a model that adjusted for all variables in Table 2, latency to product use and creatinine. For urinary metabolites, inputs to the model were divided by the ratio of observed to covariate-adjusted creatinine; <sup>†</sup>Sum of cotinine, nicotine, trans-3'-hydroxycotinine, cotinine N-oxide, nicotine 1'-oxide, norcotinine, norcotinine measured in urine; <sup>‡</sup>Measured in saliva (all other metabolites measured in urine); NRT – nicotine replacement therapy; EC – electronic cigarette

Parent Compound	Biomarker/Metabolite	Smokers			Ex-smokers		<i>P</i> -value
		Cigarette-only (N=37)	Dual cigarette-NRT users (n=36)	Dual cigarette-EC users (n=36)	NRT-only users (n=36)	EC-only users (n=36)	
Geometric mean (95% confidence interval)							
Tobacco Alkaloids (saliva)		ng/ml					
Nicotine	Nicotine‡	260.3 (189.1-358.4)	147.2 (102.1-212.0)	299.4 (193.2-464.0)	158.5 (97.1-258.6)	184.4 (125.2-271.6)	0.003 <sup>†</sup>
	Cotinine‡	174.8 (105.1-290.8)	67.1 (39.1-115.1)	149.2 (95.8-232.3)	83.9 (45.8-153.7)	179.6 (118.1-273.0)	0.134
Tobacco Alkaloids (urine)		nmol or pmol/mg creatinine§					
Nicotine	Total nicotine equivalents‡	21.1 (14.0-31.8)	8.5 (3.9-18.4)	28.8 (16.6-49.8)	6.3 (2.9-14.1)	25.0 (14.8-42.0)	0.204
	trans-3'-Hydroxycotinine	8.5 (5.1-14.3)	3.2 (1.4-7.4)	10.9 (6-19.8)	2.8 (1.2-6.3)	11.4 (6.5-19.9)	0.442
	Cotinine	5.9 (3.8-9.3)	1.8 (0.7-4.4)	8.2 (4.6-14.8)	1.4 (0.6-3.5)	7.5 (4.5-12.4)	0.188
	Nicotine	1.9 (1.2-3.3)	1.2 (0.5-2.5)	4 (2.3-7.1)	0.8 (0.3-1.7)	2.5 (1.5-4.2)	0.088
	Cotinine N-oxide	0.6 (0.4-1.0)	0.2 (0.1-0.5)	0.8 (0.5-1.4)	0.2 (0.1-0.4)	0.8 (0.5-1.3)	0.254
	Nicotine 1'-oxide	0.7 (0.4-1.1)	0.4 (0.2-0.8)	1.3 (0.7-2.2)	0.2 (0.1-0.6)	0.9 (0.5-1.6)	0.166
	Norcotinine	0.2 (0.1-0.3)	0.1 (0.1-0.2)	0.3 (0.2-0.5)	0.1 (0.1-0.1)	0.2 (0.1-0.3)	0.161
	Nornicotine	0.2 (0.1-0.2)	0.1 (0.1-0.2)	0.2 (0.1-0.4)	0.1 (0.1-0.1)	0.1 (0.1-0.2)	0.022 <sup>†</sup>
Anabasine	Anabasine§	17.0 (11.2-25.8) <sup>d,e</sup>	11.1 (6.3-19.4)	25.5 (16.3-40.1) <sup>d,e</sup>	5.5 (3.5-8.7) <sup>a,c</sup>	6.2 (4.1-9.5) <sup>a,c</sup>	<0.001
Anatabine	Anatabine§	26.0 (16.3-41.4) <sup>d,e</sup>	14.9 (7.6-29.2) <sup>d</sup>	36.0 (22.0-59.1) <sup>d,e</sup>	3.8 (2.4-6.2) <sup>a,b,c</sup>	4.6 (2.8-7.6) <sup>a,c</sup>	<0.001
Tobacco Specific <i>N</i> -Nitrosamines		pg/mg creatinine					
4-							
(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)‡	53.4 (36.6-77.8) <sup>d,e</sup>	24.4 (13.2-45.1) <sup>d,e</sup>	44.5 (28.5-69.4) <sup>d,e</sup>	4.83 (2.79-8.34) <sup>a,b,c,e</sup>	1.47 (1.02-2.12) <sup>a,b,c,d</sup>	<0.001
<i>N'</i> -nitrosoanabasine	<i>N'</i> -nitrosoanabasine (NAB)	6.17 (4.31-8.82) <sup>d,e</sup>	3.64 (2.20-6.02) <sup>d,e</sup>	6.02 (4.15-8.73) <sup>d,e</sup>	1.52 (1.09-2.12) <sup>a,b,c</sup>	1.07 (0.79-1.47) <sup>a,b,c</sup>	<0.001
<i>N'</i> -nitrosoanatabine	<i>N'</i> -nitrosoanatabine (NAT)	32.8 (20.5-52.5) <sup>d,e</sup>	11.8 (5.77-24.0) <sup>d,e</sup>	30.8 (18.5-51.1) <sup>d,e</sup>	2.95 (1.81-4.81) <sup>a,b,c</sup>	1.79 (1.21-2.67) <sup>a,b,c</sup>	<0.001
Volatile Organic Compounds		ng/mg creatinine					
Acrolein	N-Acetyl-S-(2-carboxyethyl)-L-cysteine (CEMA)	119.8 (88.2-162.9) <sup>d,e</sup>	136.1 (100.7-184) <sup>d,e</sup>	141.8 (106.7-188.4) <sup>d,e</sup>	67.8 (49.3-93.2) <sup>a,b,c</sup>	54.6 (41.7-71.4) <sup>a,b,c</sup>	<0.001
	N-Acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA)‡	488.4 (345.1-691.2) <sup>d,e</sup>	499.7 (350-713.5) <sup>d,e</sup>	574.5 (429.1-769.2) <sup>d,e</sup>	236.1 (168.1-331.6) <sup>a,b,c</sup>	175.3 (124-247.8) <sup>a,b,c</sup>	<0.001
Acrylamide	N-Acetyl-S-(2-carbamoylethyl)-L-cysteine (AAMA)‡	65.6 (50.6-85.1) <sup>d,e</sup>	52.5 (40.4-68.4) <sup>d,e</sup>	82.4 (66.1-102.8) <sup>d,e</sup>	33.6 (25.8-43.7) <sup>a,b,c</sup>	29.3 (22.3-38.3) <sup>a,b,c</sup>	<0.001
	N-Acetyl-S-(2-carbamoyl-2-hydroxyethyl)-L-cysteine (GAMA)	18.5 (14.7-23.3) <sup>d,e</sup>	16.8 (13.1-21.5)	24.3 (19.6-30.2) <sup>d,e</sup>	12.1 (9.5-15.5) <sup>a,c</sup>	10.0 (7.6-13.2) <sup>a,c</sup>	<0.001

Parent Compound	Biomarker/Metabolite	Smokers			Ex-smokers		<i>P</i> -value
		Cigarette-only (N=37)	Dual cigarette-NRT users (n=36)	Dual cigarette-EC users (n=36)	NRT-only users (n=36)	EC-only users (n=36)	
		Geometric mean (95% confidence interval)					
Acrylonitrile	N-Acetyl-S-(2-cyanoethyl)-L-cysteine (CYMA)‡	49.2 (32.9-73.6) <sup>d,e</sup>	28.4 (15.6-51.9) <sup>d,e</sup>	51.6 (33.6-79.2) <sup>d,e</sup>	3.7 (2.1-6.5) <sup>a,b,c</sup>	1.4 (1.1-1.9) <sup>a,b,c</sup>	<0.001
Benzene	<i>trans,trans</i> -Muconic acid (MU)	78.6 (58.2-106.2)	106.8 (72.7-157.0)	135.0 (102.3-178.1) <sup>e</sup>	131.8 (94.1-184.5)	55.2 (42.3-71.9) <sup>c</sup>	0.002
1,3-Butadiene	N-Acetyl-S-(phenyl)-L-cysteine (PMA)	0.64 (0.48-0.84) <sup>c</sup>	0.44 (0.30-0.63) <sup>c</sup>	1.43 (1.11-1.83) <sup>a,b,e</sup>	0.52 (0.37-0.71)	0.74 (0.55-0.98) <sup>c</sup>	<0.001
	N-Acetyl-S-(3,4-dihydroxybutyl)-L-cysteine (DHBMA)	202.7 (162.8-252.3) <sup>e</sup>	204.3 (162.3-257.3) <sup>e</sup>	294.9 (242.9-358.0) <sup>e</sup>	204.2 (156.9-265.9)	156.3 (126.0-193.8) <sup>a,b,c</sup>	<0.001
	N-Acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine (MHBMA3)‡	29.8 (19.9-44.8) <sup>d,e</sup>	23.9 (15.1-37.9) <sup>d,e</sup>	36.6 (25.4-52.6) <sup>d,e</sup>	7.67 (5.08-11.6) <sup>a,b,c</sup>	4.44 (3.42-5.78) <sup>a,b,c</sup>	<0.001
Carbon disulfide	2-Thioxothiazolidine-4-carboxylic acid (TTCA)	6.03 (4.40-8.27)	13.8 (8.79-21.7)	9.95 (6.85-14.5)	13.4 (9.07-19.7)	6.84 (4.33-10.8)	0.015†
Crotonaldehyde	N-Acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine (HPMMA)	804.2 (563.8-1147.1) <sup>d,e</sup>	735.3 (495.2-1091.7) <sup>d,e</sup>	1199.5 (881.9-1631.6) <sup>d,e</sup>	366.3 (266.0-504.5) <sup>a,b,c</sup>	235.9 (179.1-310.7) <sup>a,b,c</sup>	<0.001
Cyanide	2-Aminothiazoline-4-carboxylic acid (ATCA)	91.2 (69.6-119.5) <sup>e</sup>	107.1 (79.4-144.5) <sup>d,e</sup>	132.3 (97.8-179.0) <sup>d,e</sup>	102.0 (72.6-143.4)	55.3 (41.0-74.5) <sup>a,b,c</sup>	0.013
N,N-Dimethylformamide	N-Acetyl-S-(N-methylcarbamoyl)-L-cysteine (AMCC)	162.2 (120.6-218.1) <sup>e</sup>	138.5 (95.4-201.2) <sup>e</sup>	176.3 (129.1-240.5) <sup>e</sup>	100.2 (72.4-138.7)	60.8 (44.4-83.3) <sup>a,b,c</sup>	<0.001
Ethylene oxide, acrylonitrile, vinyl chloride	N-Acetyl-S-(2-hydroxyethyl)-L-cysteine (HEMA)‡	0.81 (0.61-1.07) <sup>d,e</sup>	0.81 (0.55-1.18)	1.15 (0.84-1.57) <sup>d,e</sup>	0.64 (0.48-0.84) <sup>a,c</sup>	0.42 (0.32-0.55) <sup>a,b,c</sup>	<0.001
Propylene oxide	N-Acetyl-S-(2-hydroxypropyl)-L-cysteine (2HPMA)	41.1 (30.4-55.6) <sup>e</sup>	47.3 (35.6-63.0) <sup>e</sup>	68.9 (52.6-90.4) <sup>d,e</sup>	37.4 (28.7-48.9) <sup>c</sup>	29.3 (21.9-39.3) <sup>a,b,c</sup>	<0.001
Styrene	Mandelic acid (MA)	188.6 (147.4-241.2) <sup>e</sup>	198.7 (153.8-256.7) <sup>e</sup>	227.2 (181.1-284.9) <sup>e</sup>	173.0 (127.3-235.3)	100.8 (78.2-129.9) <sup>a,b,c</sup>	<0.001
	N-Acetyl-S-(1 and 2-phenyl-2-hydroxyethyl)-L-cysteine (PHEMA)	0.75 (0.57-0.98)	0.82 (0.56-1.18)	1.09 (0.8-1.48) <sup>e</sup>	0.75 (0.55-1.00)	0.48 (0.36-0.63) <sup>c</sup>	0.001
Styrene, ethylbenzene	Phenylglyoxylic acid (PGA)	88.0 (62.6-123.8)	129.9 (92.1-183.3) <sup>e</sup>	124.5 (91.1-170.0)	88.1 (60.6-128.2)	71.1 (53.7-94.1) <sup>b</sup>	0.007
Xylene	2-Methylhippuric acid (2MHA)	41.9 (30.1-58.4) <sup>d,e</sup>	36.3 (23.9-55.2) <sup>d,e</sup>	56.9 (41.8-77.4) <sup>d,e</sup>	19.6 (13-29.7) <sup>a,b,c</sup>	10.5 (7.80-14.2)	<0.001
	3- + 4-Methylhippuric acids (34MHA)	266.5 (182.1-390.1) <sup>d,e</sup>	181.1 (119.7-274.0) <sup>d,e</sup>	273.2 (201.1-371.0) <sup>d,e</sup>	76.3 (48.8-119.4) <sup>a,b,c</sup>	51.4 (38.5-68.6) <sup>a,b,c</sup>	<0.001

588 \*Data presented are log-transformed raw values (for urinary metabolites also standardized for creatinine). Statistical comparisons were carried out on non-transformed data, adjusted for all  
589 variables in Table 2, latency to product use and creatinine; †Overall differences but no significant (Sidak-corrected) difference in post-hoc test; ‡Non-log transformed data shown in Figures 1  
590 and 2; §Indicates pmol/mg creatinine; <sup>a, b, c, d, e</sup> indicates statistically significant (Sidak-corrected) difference (p<0.05) (a) cigarette-only smokers, (b) dual cigarette-NRT users, (c) dual cigarette-  
591 EC users, (d) NRT-only users, and (e) EC-only users; NRT – nicotine replacement therapy; EC – electronic cigarette; P-value – omnibus test result, adjusted for the number of reported comparisons  
592 in this table using the false discovery rate (46)

Biomarker/Metabolite*	Limit of detection	All samples	Smokers			Ex-smokers	
			Cigarette-only (N=37)	Dual cigarette-NRT users (n=36)	Dual cigarette-EC users (n=36)	NRT-only users (n=36)	EC-only users (n=36)
Percent							
Nicotine <sup>†</sup>	10 ng/mL	1.1	0.0	0.0	2.8	2.8	0.0
Cotinine <sup>†</sup>	10 ng/mL	14.4	13.5	16.7	5.6	27.8	8.3
trans-3'-Hydroxycotinine	0.03 ng/mL	0.0	0.0	0.0	0.0	0.0	0.0
Cotinine	0.03 ng/mL	0.0	0.0	0.0	0.0	0.0	0.0
Nicotine	10.5 ng/mL	11.0	2.7	13.9	5.6	30.6	2.8
Cotinine N-oxide	2 ng/mL	7.7	0.0	13.9	2.8	19.4	2.8
Nicotine 1'-oxide	2.5 ng/mL	8.8	0.0	13.9	2.8	25.0	2.8
Norcotinine	2.5 ng/mL	11.6	0.0	22.2	5.6	27.8	2.8
Nornicotine	1.1 ng/mL	17.7	5.4	30.6	11.1	33.3	8.3
Anabasine	0.5 ng/mL	29.3	10.8	36.1	13.9	55.6	30.6
Anatabine	0.4 ng/mL	29.3	5.4	27.8	11.1	61.1	41.7
N-Acetyl-S-(2-carboxyethyl)-L-cysteine (CEMA)	8 ng/mL	2.8	0.0	2.8	0.0	5.6	5.6
N-Acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA)	13 ng/mL	0.0	0.0	0.0	0.0	0.0	0.0
N-Acetyl-S-(2-carbamoylethyl)-L-cysteine (AAMA)	2.2 ng/mL	0.0	0.0	0.0	0.0	0.0	0.0
N-Acetyl-S-(2-carbamoyl-2-hydroxyethyl)-L-cysteine (GAMA)	9.4 ng/mL	30.9	16.2	25.0	19.4	41.7	52.8
N-Acetyl-S-(2-cyanoethyl)-L-cysteine (CYMA)	0.5 ng/mL	2.2	0.0	0.0	0.0	2.8	8.3
trans,trans-Muconic acid (MU)	20 ng/mL	6.6	2.7	2.8	2.8	5.6	19.4
N-Acetyl-S-(phenyl)-L-cysteine (PMA)	0.6 ng/mL	56.9	37.8	94.4	30.6	86.1	36.1
N-Acetyl-S-(3,4-dihydroxybutyl)-L-cysteine (DHBMA)	5 ng/mL	0.0	0.0	0.0	0.0	0.0	0.0



Biomarker/Metabolite*	Limit of detection	All samples	Smokers			Ex-smokers	
			Cigarette-only (N=37)	Dual cigarette-NRT users (n=36)	Dual cigarette-EC users (n=36)	NRT-only users (n=36)	EC-only users (n=36)
					Percent		
N-Acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine (MHBMA3)	0.6 ng/mL	0.0	0.0	0.0	0.0	0.0	0.0
2-Thioxothiazolidine-4-carboxylic acid (TTCA)	3.5 ng/mL	28.2	29.7	22.2	41.7	13.9	33.3
N-Acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine (HPMMA)	2 ng/mL	0.0	0.0	0.0	0.0	0.0	0.0
2-Aminothiazoline-4-carboxylic acid (ATCA)	15 ng/mL	7.2	0.0	8.3	5.6	5.6	16.7
N-Acetyl-S-(N-methylcarbamoyl)-L-cysteine (AMCC)	5.5 ng/mL	0.6	0.0	0.0	2.8	0.0	0.0
N-Acetyl-S-(2-hydroxyethyl)-L-cysteine (HEMA)	0.6 ng/mL	48.6	32.4	41.7	27.8	61.1	80.6
N-Acetyl-S-(2-hydroxypropyl)-L-cysteine (2HPMA)	1.3 ng/mL	0.0	0.0	0.0	0.0	0.0	0.0
Mandelic acid (MA)	12 ng/mL	1.1	0.0	0.0	0.0	2.8	2.8
N-Acetyl-S-(1 and 2-phenyl-2-hydroxyethyl)-L-cysteine (PHEMA)	0.7 ng/mL	61.3	48.6	58.3	55.6	63.9	80.6
Phenylglyoxylic acid (PGA)	12 ng/mL	9.9	10.8	11.1	8.3	11.1	8.3
2-Methylhippuric acid (2MHA)	5 ng/mL	0.0	0.0	0.0	0.0	0.0	0.0
3- + 4-Methylhippuric acids (34MHA)	8 ng/mL	1.7	0.0	0.0	0.0	2.8	5.6
4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	0.6 pg/mL	6.6	0.0	2.8	0.0	8.3	22.2
N'-nitrosoanabasine (NAB)	4.0 pg/mL	47.0	8.1	38.9	25.0	80.6	83.3
N'-nitrosoanatabine (NAT)	1.6 pg/mL	43.1	5.4	41.7	13.9	75.0	80.6

\*Urinary biomarkers, unless where indicated; \*Measured in saliva